EXHIBIT D

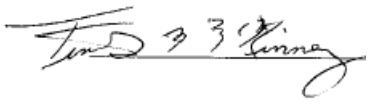
UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC. **PELVIC REPAIR SYSTEM** **PRODUCTS LIABILITY LITIGATION**	**Master File No. 2:12-MD-02327** **MDL No. 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

DEFENSE EXPERT GENERAL REPORT

of Timothy McKinney, M.D.:

Prepared by:



Timothy McKinney, M.D.

March 2, 2016

Report re: Prolene Soft (Gynemesh PS)

This report contains a summary of my qualifications, education, training, and experience, a statement of my opinions that I have formed to date, the bases for those opinions, and the information I considered in forming my opinions. All of my opinions are based on my education, training, clinical experience, the pertinent medical literature, discussions with colleagues, and other materials I have reviewed. Materials that support my findings and opinions, including documents that I have reviewed, are identified either in this report or are listed in the attached reliance materials list.

All of the opinions I express in this report are held to a reasonable degree of medical and scientific probability and certainty. If I receive additional information after signing this report but before trial, I may form additional or different opinions.

I. Background

a. Education, Training, and Experience

I attended Bucknell University, graduating with a Bachelor of Science degree in biochemistry.

I graduated from Rutgers Medical School in New Jersey in 1987. I did my internship and residency in OB/Gyn at Cooper Hospital University Medical Center in Camden, NJ from 1987 to 1991. I then did a fellowship in urogynecology at Pennsylvania Hospital (part of U of Pennsylvania) in Philadelphia.

I became a Diplomate of the American Board of OB/ GYN in 1994 and am subspecialty board certified in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) in August 2013. I am an active member of the American Urological Association (AUA), the American Urogynecology Society(AUGS), Society of Urodynamic and Female Urology (SUFU), International Urogynecology Association (IUGA), European Association of Urology (EAU), International Continence Society (ICS), ISGL, and American Association of Gynecological Laparoscopy (AAGL). I am a Professor at Drexel University College of Medicine in Philadelphia, Pennsylvania and part of the fellowship training program for MIS and FPMRS. I taught 100's of courses on pelvic reconstruction, both vaginal, laparoscopic and open, incontinence, pelvic/ vaginal/ bladder pain evaluation, diagnosis, and treatment. I published an abstracts as early as 1994 about a comparative study of laparoscopic retropubic urethropexy with Prolene mesh and classic Burch suspension, addressing 56 cases in which we had one-year follow up. I authored several chapters about pelvic floor surgery and incontinence surgery one which was published in May of 2007 . We discussed the theory that isolated breaks in the endopelvic fascia as described by Cullen Richardson, MD were the key to pelvic floor support and needed to be addressed during reparative pelvic surgery. I was a co- author on the first North American experience/ data on TVT with results of 95 cases published in 1999. I had two abstract/poster presentations about my experience with Gynemesh PS. The first covered '02 – '05, patients. We updated it in '06, but there were some Prolifts in the 2006 version.

In addition to my public literature, when I was practicing full time my website had a discussion about vaginal repair with mesh, publications of the IUGA findings and a commentary on the FDA safety communication released in July, 2011 all to educate my patients and other doctors better. In January, 2013 my partner and I were chosen as one of the few sites to participate by AMS in their post-marketing studies on Elevate (522). We were chosen to do all 3 arms of the study, anterior elevate, posterior elevate and native tissue repairs for our skills and qualifications.

I at one time had a consulting role with Ethicon regarding pelvic surgery and mesh. For example, I was a contributor to the resource monograph. I was invited to panel discussions. I was a preceptor.

I was also a consultant to AMS in an important period of time after the 2011 FDA warning.

It is clear that pelvic surgeons adopted mesh into the pelvic space from the success of hernia surgeons. Gynecologic surgeons were using hernia mesh long before products like Gynemesh PS were launched. I not only used them for POP, but for mid-urethral sling procedures as well.

I cut and shaped the Gynemesh PS based on my evaluation of each patient and my knowledge of anatomy to best suit my patients' needs. I used it for site specific vaginal support repairs, sacrocolpopexy and for a modified burch procedure for incontinence. Burch use was replaced by the TVT and I was one of the 1st to learn Dr. Ulmsten's technique and practiced and studied TVT on cadavers due to my access to use cadavers in courses and then IMET a company I helped start to teach anatomy. It's also where I gained extensive experience with the augmentations using graft materials before applying that knowledge to the patients. I consider myself one of the world's foremost experts in pelvic anatomy.

My curriculum vitae is attached to this report.

b. Clinical Experience & Personal Experience with Stress Urinary Incontinence and Pelvic Organ Prolapse Treatments

I have a special focus in female pelvic medicine and surgery. Over the course of my career, I have performed various types of native tissue surgery and have a large study of use of the uterosacral ligaments for support and worked with Cullen Richardson on pioneering site specific repairs. I helped start a company to teach anatomy on unembolmed cadavers to do a more anatomical repair then what was in the past. The frustration to all of us is that native tissue, which in this population of patients is inherently poor, had an unacceptable failure rate. Thus, as with the surgeons' frustration over failures in hernias they started using and augmenting their repairs with mesh material. In 1995 was the 1st prospective randomized trial looking at incontinence procedures, Bergman's. He found the standard procedure of Kelly Plication to have a 37% 5 year success rate. The Stamey needle suspension had a miserable 42 % success. The Burch abdominal incision procedure had an 82% success. The use worldwide of a minimally invasion surgery for stress incontinence was launched in 1994 and brought to the USA

in 1996 has a high rate of success 83-94% with less risks. I used surgery utilizing mesh, such as Ethicon's TVT and TVT-O mid-urethral slings, AMS Monarch, miniarc, retroarc, Elevate, Uretex by Bard, Vesica In situ sling, Stamey cystourethropexy, sacrocolpopexy and Burch procedures. I have also performed laparoscopic, robotic as well as open sacrocolpopexies using prolene meshes. We crafted these hernia mesh materials for years before companies tried to standardize the materials and researching to try to find that perfect material. Til today there is not the perfect material and will be even less likely to develop them going forward. I have also performed various types of native tissue surgeries autologous and zenografts and surgeries utilizing mesh, including Prolene Soft mesh, to treat pelvic organ prolapse and other hernias.

c. Teaching & Research

I served as a faculty member teaching surgeons how to perform better surgical techniques and understand pelvic anatomy and its relationship to support. I have performed research in the field of incontinence and bladder disorders, contributing to numerous studies on incontinence, prolapse, pelvic pain attributed to prolapse, Interstitial cystitis vulvadynia and vaginismus. I have several chapters on anatomy and prolapse surgery, as well as incontinence. Through my research I created a better pressure sensing technology in TDOC urodynamic catheters to better predict outcomes.

d. Litigation Consulting Work

During the previous four years, I have testified as an expert witness at trial or by deposition in less than a handful of cases.

I am being compensated $650.00 per hour for my study and work in this case.

II. Pelvic Organ Prolapse

a. Definition, Mechanism of Action, and Prevalence

Pelvic organ prolapse, overactive bladder, and urinary incontinence affect more women than diabetes, heart disease, or arthritis. The overall lifetime risk for undergoing surgery for pelvic organ prolapse is 11.1% or 1 in 9 women by the age of 80. The risk of surgery increases to 16% status post hysterectomy. It is the leading cause of women being institutionalized and has a tremendously negative affect on the quality of life leading to depression, seclusion loss of identity for these patients.

The proposed mechanism of action for the development of pelvic organ prolapse begins with damage of the pelvic support structures from the inside out. Tears in the fascial support lead to hernias of the pelvic floor as well as damage to the levator ani muscles and nerves which decreases muscle tone and strength, leading to muscular disuse atrophy causing descent and a widened levator hiatus. Increased intra-abdominal pressure is then unopposed, placing additional forces on the connective tissue, which tears over time. Pelvic organ prolapse is most common in the anterior compartment and then posterior compartment as well as apical prolapse

making up the common site-specific defects. A combination of one or all make up the problem of prolapse and when one are is effected a progression of the disease often follows leading to worsening symptoms over the years.

b. Risk Factors for Pelvic Organ Prolapse and Stress Urinary Incontinence

Smoking: Women who smoke have a 2-3 times more likely incidence of urinary incontinence 2nd to chronic obstructive pulmonary disease and increasing abdominal pressures from coughing and changes in connective tissue biochemical matrix weaking support and causing pelvic organ prolapse. This was true in even in my research publication on uterosacral ligament with myself and Robert Rogers, MD where smoking was the only statistically significant risk fact of prolapse.

Obesity: Increasing body mass index correlates to an increase in the symptoms of urinary incontinence and pelvic organ prolapse.

Menopause: Decreasing serum levels of estrogen are known to increase the incidence of both stress incontinence and decrease the integrity of the pubocervical fascia of the vagina by decreasing vascularity and thickness of the tissues. Postmenopausal decreased estrogen levels lead to urogenital atrophy with the increased risk of infections of the urinary tract and changing of the vaginal pH. It is also the single most common cause of sexual pain in menopausal or even women on birth control which is predominantly progesterone driven.

Pregnancy and Childbirth: Damage sustained to the fascia, ligaments, muscles and nerves of the pelvic floor significantly increase the risk of both stress and urge incontinence and pelvic organ prolapse. There is an 11-fold increased risk of pelvic organ prolapse with three or more vaginal deliveries compared to nulliparous women. The weight of the infant contributes to prolapse with an increase of 10% per pound weight of the infant. Brazil has the lowest prolapse and incontinence rate in the world and has the highest c-section rate in the world. They believe in protecting the pelvic floor integrity.

Race: Increasing incidence of prolapse occurs from African-American < Asian<Caucasian<Hispanic. Hispanic women have the highest risk of pelvic organ prolapse

Age: Pelvic organ prolapse levels increase with each decade for women between the ages of 20 and 59 years and the incidence of prolapse requiring surgery also has a dramatic increase with each successive decade.

Congenital factors: Women with prolapse having an abundance of the weak or type III collagen in the pubocervical and rectovaginal fascia with a higher degree of joint hypermobility with associated collagen vascular disorders also increase the incidence and severity of prolapse.

Hysterectomy: The lifetime risk of prolapse post-hysterectomy is 16% with no specific technique increasing risk. The incidence of women developing severe prolapse after hysterectomy is to 3.6 birth 1000 women years and if the hysterectomy was performed with initial complaints of prolapse or rate is as high as 15 per 1000 women years.

Stress Urinary Incontinence: 62% of women with prolapse also report stress incontinence, and 63% of women with stress incontinence have associated prolapse. 30% of women will undergo repeat surgery for recurrent prolapse over their lifetime especially if no augmentation of their support is done..

III. Treatment Options for Pelvic Organ Prolapse

a. Nonsurgical Options for Treatment of Pelvic Organ Prolapse

Conservative management of pelvic organ prolapse is the avoidance of pelvic and abdominal straining in the form of heavy lifting or squatting. Patients can also be treated with physical therapy using biofeedback, Kegel exercises, estrogen vaginal supplementation, and pessaries.

b. Surgical Options for Treatment of Pelvic Organ Prolapse

Surgical corrections of pelvic organ prolapse have many different approaches—from either vaginal or abdominal and involve open incisions or laparoscopic techniques. For relatively simple cystocele and rectocele repair, native tissue plication with absorbable or permanent sutures can be accomplished. The paravaginal repair with absorbable sutures has a much higher failure rate and is why non-absorbable is recommended often times Prolene. A 30-50% 5-year failure rate based on multiple studies is noted and the reason surgeons began using materials to augment repair including Thomas Julian with Marlex polypropylene mesh who was one of my mentors, and Glen Hurt, utilizing cadaveric fascial sheets who also was my mentor. They all had one thing in common, frustration over the failure of native tissue repairs. Sacrospinous ligament fixation and uterosacral ligament repairs have higher rates of success, but also higher rates of complications including ureter damage and obstruction, hemorrhage, chronic pelvic pain, dyspareunia, urinary retention, and injury to adjacent organs such as the bladder, rectum, and vessels. Abdominal sacrocolpopexy performed either open, laparoscopically or robotically are also an option. It has the highest rate of success but also a significant rate of complications. The sacrocolpopexies have used permanent mesh materials for over 60 years. Native tissue repairs have risks of chronic vaginal pain (when I was 1st trained in the late 80's it was associated with about 40% dyspareunia and was one of the reasons I became interested in this field). Anterior and posterior colporrhaphies were anatomically unsound and shortening of the vagina, dyspareunia, bleeding, infection, exposure of the suture materials even years later were also common . Site specific repairs as described by Cullen Richardson and learned by hundreds of cadaveric dissections where leaving anatomically more normal vaginas, but as with all reconstructive surgeries have the above risks and native tissue has increased failure especially anterior and apical.

Due to the high rate of failure using native tissue plication and suture fixation, biologic and synthetic materials have been incorporated into repairs for over 30 years. Cadaveric fascia, autologous fascia, or synthetic meshes have been incorporated to augment the repair in an attempt to increase the anatomic long-term success. The augmented repairs have the same potential complications as native tissue plications, with additional possible complications of

mesh exposure, extrusion much like the expulsion, exposure and extrusion of suture material. The rate of vaginal mesh exposure varies from 3% to 34% in various studies, and with small areas of exposure topical estrogen and time may be all that is required for treatment. For larger areas of exposure or pain, local excision can be performed using either local anesthetic or general anesthesia. Mesh excision can be performed in the office setting, or an outpatient surgery center, as well as hospitals. Entrapped nerve pain can in the majority of cases be treated with in office Nerve Blocks, Neurolysis and decompression with hydrodissection with needle injections. Sometimes local steroids also work with physiotherapy. If this fails excision or total explant needs to be done, but is rare in my hands.

c. Pelvic Organ Prolapse's Economic Impact and Impact on Quality of Life

Pelvic organ prolapse can have significant adverse effects on the quality of women's lives. It can be painful, can negatively affect women's relationships, and it can cause patients to isolate themselves socially and be less active. Symptoms include a feeling that something is falling out of the vagina, a pulling sensation in the pelvic area, lower back pain, and a sensation of pressure of fullness from organs pressing against the vaginal walls. Patients with rectocele often have constipation as a result. The costs of pelvic organ prolapse surgery was calculated to be over a billion dollars in 1997.[1]

IV. Ethicon's Prolene™ Soft Mesh Product

a. Historical Background of Surgical Use of Mesh

Polypropylene monofilament suture was introduced into surgery in 1958 by Usher, and has become the main material used in tissue repair. Polypropylene sutures have been used for over 55 years and are biologically compatible with human tissue. Polypropylene hernia mesh has been and continues to be the standard of care for the last thirty years for abdominal wall hernia repair. Polypropylene mesh has been used in open abdominal sacrocolpopexies since the 1960s. The advantage of mesh is augmentation and strength during the healing process with the incorporation of collagen fibers into the material to provide lasting support. I have performed mesh hernia repairs and never had a patient develop an infection of the mesh itself or rejection of the material.

Polypropylene meshes have been used in the vagina for almost 60 years. Surgeons have turned to synthetic materials to augment healing and reinforcement of poor-quality native fascia and collagen that has deteriorated both by years and trauma. Due to the high failure rate of suture repairs for vaginal prolapse, mesh grafts have been developed to address the problem in the same manner as hernia repairs of the abdominal wall.

b. The Development of Prolene™ Soft Mesh

[1] Subak LL, Cost of pelvic organ prolapse surgery in the United States. Obstet Gynecol 2001 Oct;98(4):646–51.

Prolene™ Soft is a product developed by Ethicon for hernia repair, and is indicated for "the repair of hernia or other fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result." Prolene Soft mesh was introduced in 2000. It is a monofilament, knitted, macroporous, synthetic mesh that comes in sheets that can be cut by the surgeon to the desired shape based on the surgery being performed and the patient's anatomy. I had used it for years before the kits were available. It is made of knitted filaments of extruded polypropylene identical in composition to that used in Prolene polypropylene sutures that have been used in various surgical specialties for more than 50 years, and it includes blue Prolene monofilaments to produce contrast striping that makes the mesh more visible when implanted. The IFU notes that "The mesh is constructed of reduced diameter monofilament fibers, knitted into a unique design that results in a mesh that is approximately 50 percent more flexible than standard PROLENE mesh." The knitting process provides for elasticity in both directions—which "allows adaptation to various stresses encountered in the body"—and "permits the mesh to be cut into any desired shape or size without unraveling." The IFU also notes:

> Animal studies show that implantation of PROLENE mesh elicits a minimal to slight inflammatory reaction, which is transient and followed by the deposition of a thin fibrous layer of tissue which can grow through the interstices of the mesh, thus incorporating the mesh into adjacent tissue. The mesh remains soft and pliable, and normal wound healing is not noticeably impaired. The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.

The mesh is a Type I mesh, per the biomaterial classification published by PK Amid in 1997, as it contains pores larger than 75 microns, "which is the required pore size for admission of macrophages, fibroblasts (fibroplasia), blood vessels (angiogenesis) and collagen fibers into the pores." (Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997;1:15–21.) The pore size of Prolene soft is approximately 2,500 µm, and thus allows for excellent tissue integration and the passing of leukocytes and macrophages to clear any pathogens. This was the type of research that brought to light not to use Goretex or Marlex in these spaces.

The year Prolene Soft was introduced, a group of surgeons in France calling themselves the "TVM Group" started to study the use of non-absorbable synthetic mesh in urogenital prolapse repair, which was prompted by the 20–30% prolapse recurrence rates following traditional native tissue repairs. The TVM Group selected Prolene Soft mesh, as they found it to be the most appropriate mesh for the transvaginal approach of the surgical repair of prolapse at that time. They noted that the Prolene Soft was "a carefully selected and tested synthetic material."[2] Over time there was an evolution of technology going on to find the "perfect " replacement of the fascial support.

On June 6, 2000 Brigitte Hellhammer of Ethicon (R&D Europe) wrote an internal document about meshes and pelvic floor repair based on a literature review and conversations with surgeons. This was the internal impetus for creating Gynemesh PS. She noted that

[2] Berrocal J, et al., Conceptual advances in the surgical management of genital prolapse—The TVM technique emergence. J Gynecol Obstet Biol Reprod 2004;33:577–87.

abdominal, laparoscopic and vaginal approaches to POP repair were all common and that there was no internationally recognized gold standard procedure. She also interviewed 23 surgeons, 11 of whom had used mesh for pelvic floor repair. She recommended the launch a separate mesh product for prolapse repair as a second generation Gynemesh. (It was already marketed in Europe.) Dr. Hellhammer's June, 2000 report has a substantial bibliography. She looked at 62 publications. (All are listed in the Appendix to her document.)

On November 6, 2001 Ethicon submitted its 510(K) for Gynemesh PS. The main predicate device was Prolene Soft Mesh (cleared 5/23/2000). The difference between the predicate and Gynemesh PS was only for the indication – pelvic floor repair. The other predicates were Prolene Mesh (8/9/1996) and Mersilene (pre-amendment). The following eight articles were attached to the 510(K) in Appendix 6.

1) Cundiff, et al., Abdominal Sacralcolpoperineopexy: A New Approach for Correction of Posterior Compartment Defects and Perineal Descent associated with Vaginal Vault Prolapse, American Journal of Obstetrics and Gynecology, December 1997. They studied 19 women operated between 12/1/1995 and November 30, 1996 with a modification of their standard abdominal Sacrocolpopexy. They used Mersilene to augment the repair. They concluded that their modified technique was effective for vaginal vault prolapse.

2) Diana, Treatment of Vaginal Vault Prolapse with Abdominal Sacral Colpopexy Using Prolene Mesh. The American Journal of Surgery, February 2000. Between 1994 and 1997 they operated on 15 patients for vaginal vault prolapse. They confirmed ASC with a "prolene net" as "the most valid technique… in the treatment of total vaginal vault prolapses, …"

3) Julian's 1998 paper

4) Kohli's 1998 paper

5) Migliari, Tension-Free Vaginal Mesh Repair for Anterior Vaginal Wall Prolapse, European Urology 2000. They studied 12 women but the brand of mesh isn't apparent due to poor copy quality. They simply confirmed that patients with moderate cystocele had effective treatment with mesh augmentation.

6) Nicita's 1998 paper

7) Visco, Vaginal Mesh Erosion after Abdominal Sacral Colpopexy (American Journal of Obstetrics and Gynecology, September 2001). They studied 273 women who had POP repair between March of 1992 and February of 1999 (?). It may be that this group received a mixed batch of products. In any event, the conclusion was that the rate of erosion was higher at the time the erosion shorter with combined vaginal and abdominal procedures, when compared with abdominal Sacrocolpopexy.

8) Winters, Abdominal Sacral Colpopexy and Abdominal Enterocele Repair in the Management of Vaginal Vault Prolapse. They believe that with good surgical technique they

could get long term efficacy and a low rate of complications, but mention infection, erosion, etc. as potential risks.

On January 8, 2002 FDA sent a letter to Ethicon clearing Gynemesh PS for marketing because it was substantially similar to a legally marketed predicate device. (Class 2)

In 2002, Gynemesh™ PS was introduced, and was "indicated for tissue reinforcement and long-lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment is intended, either as mechanical support or bridging material for the fascial defect." Such was the hernia. Prolene Soft and Gynemesh™ PS are identical meshes with different indications for use. A surgeon choosing to use Prolene Soft mesh for vaginal prolapse repair can do so from either a transabdominal or vaginal approach.

c. The Safety and Efficacy of Prolene™ Soft/ Gynemesh PS Mesh

Review of scientific reports of the use of Gynemesh and pelvic reconstructive surgery date back to 2001. De Tayrac described 36 patients undergoing cystocele repair using Gynemesh with 13 month follow-up and 100% success with one mesh excision under local anesthesia for non-symptomatic exposure.[3]

Several studies demonstrate the versatility of Prolene Soft mesh, describing its use in various gynecologic procedures other than transvaginal procedures. Weiden described up to four-year follow-up of abdominal sacrocolpopexy and Sacrohysteropexy using Gynemesh with bone anchoring and reported excellent anatomical results and low complication rates. This study is indicative of the many different uses to which the product was being placed.[4] Agarwala describes in 2007 the use of Gynemesh for laparoscopic sacralcolpopexy for recurrent prolapse of the apex or severe uterine prolapse. 74 patients were treated with Gynemesh. Subjective and objective cure was 97 and 100%, respectively. There were no cases of graft exposure or recurrence with a median follow-up of 24 months.[5]

Lucente in 2004 described 160 patients undergoing vaginal or abdominal/vaginal repair with a less than 10% exposure rate of which most were treated in the office and success of 76% in reducing the prolapse to stage 0-1. The authors concluded that POP repair using GYNEMESH PS "is safe, with a low rate of significant mesh-related complications."[6] In 2006, Ali and colleagues described 108 patients undergoing anterior colporrhaphy with Gynemesh PS

[3] De Tayrac R, et al., Cystocele Repair with a Fixation-Free Prosthetic Polypropylene Mesh. Abs. 2001.
[4] Van der Weiden RMF, et al., Colposacropexy With Mesh or Collagen Implant and Titanium Bone Anchors Placed in Sacral Segments 3 and 4. J Pelvic Med & Surg 2003;9(1):9–14.
[5] Agarwala N, et al., Laparoscopic sacral colpopexy with Gynemesh as graft material—Experience and results. J Minimally Invasive Gynecol 2007;14:577–83.
[6] Lucente V, et al., A Clinical Assessment of GYNEMESH PS for the Repair of Pelvic Organ Prolapse. AUGS, SGS Oral Poster 55

augmentation. They encountered no intra-operative complications, a 6.6% recurrence rate, and a 6.5% exposure rate.[7]

Cosson described in 2005 the management of transvaginal mesh techniques for repair of pelvic prolapse using a vaginal approach and the use of Gynemesh. In the paper, it is described that the ideal mesh for pelvic reconstructive repair is monofilament polypropylene with large pores. The study was a continuous retrospective trial of more than two years, and was designed to identify the risk factors for exposure of mesh material and management strategies for postoperative complications. 277 patients undergoing surgery for pelvic prolapse using the TVM technique—using risk factors of body mass index, age, menopausal status, hormonal replacement therapy, previous surgical repair and hysterectomy—were included. Mesh exposure was less than 1% when the uterus was preserved. Management of mesh exposure involved local treatment combined with partial resection of the mesh if the local treatment proved inadequate. The local treatment was further enhanced with estrogen therapy.

Deffieux described in 2006 management of 34 consecutive cases of vaginal mesh erosion following transvaginal repair of cystocele using Gynemesh. 68% underwent local therapy using an estrogen cream. In 22% of cases, the mesh erosion had completely disappeared with a follow-up of 2-9 months. 59% of the symptomatic patients required partial or complete excision of the mesh with vaginal closure under general anesthesia. The surgery ranged from 15-40 minutes in duration and was successful 77% of the time. 11% of the patients undergoing a primary repair required a second operation because of recurrence. The incidence of the de novo dyspareunia was 12% with vaginal mesh exposure and 11% in those who had no exposure post operatively.[8]

Sola in a 2006 report describes 42 mesh procedures using Gynemesh PS mesh for both cystocele and rectocele, having no postoperative complications and a 95% success for cystocele and 100% success for rectocele repair.[9] Collinet and colleagues, in 2006, studied 277 patients receiving Gynemesh PS for treatment of pelvic organ prolapse using the TVM technique, and observed a mesh exposure rate of 12.27% overall in the two months following surgery, but less than 1% when the uterus was preserved.[10]

Hoenil Jo in 2007 evaluated 26 patients with stage III or IV pelvic organ prolapse for 2 years after Gynemesh vaginal repair. Success was 94% objective cure with no tissue erosion or infections noted.[11] Takeyama described in 2007 a modification of the Prolift procedure using Gynemesh PS. They implanted Gynemesh PS in 245 patients with pelvic organ prolapse and

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[7] Ali S, et al., A Prospective Randomized Trial Using Gynemesh PS for the Repair of Anterior Vaginal Wall Prolapse. Int Urogynecol J 2006;17(Supp. 2):S171–S359 (Abs. 292).
[8] Deffieux X, et al., Vaginal mesh extrusion after transvaginal repair of cystocele using a prosthetic mesh: Treatment and functional outcomes. J Gynecol Obstet Biol Reprod (Paris) 2006 Nov;35(7):678–84.
[9] Sola V, et al., Tension Free Monofilament Macropore Polypropylene Mesh (Gynemesh PS) in Female Genital Prolapse Repair. Int Braz J Urol 2006;32(4):410–15.
[10] Collinet P, et al., Transvaginal mesh technique for pelvic organ prolapse repair: mesh exposure management and risk factors. Int Urogynecol J 2006;17:315–20.
[11] Jo H, et al., Efficacy and outcome of anterior vaginal wall repair using polypropylene mesh (Gynemesh). J Obstet Gynecol Res 2007 Oct;33(5):700–04.

had no serious complications and a low recurrence and exposure rate (0.8 and 1.6%, respectively).[12] Al-Nazer and colleagues reported in 2007 the results of their study of 40 patients undergoing either anterior colporrhaphy or implantation of Prolene Soft mesh. They found both groups had improvement in their prolapse, urinary, and sexual symptoms, but the improvement was more significant in the Prolene Soft group. 95% of the Prolene Soft patients were cured, while 70% of the anterior colporrhaphy patients were cured. They also found that operative morbidity was generally lower in the Prolene Soft group.[13]

Caquant and Cosson in 2008 reported on a study of 684 patients undergoing the TVM procedure using Gynemesh PS performed between 2002-2004. The mesh exposure rate without concurrent hysterectomy was 4.7% and medical management was successful in 42% of cases. The study was limited by short-term follow up.[14] In 2008, Letouzey and colleagues reported the results of their study of 63 women undergoing cystocele repair using Gynemesh PS between 1999-2001. The patients were followed for five years, and the authors observed an 80% anatomic cure rate with an additional 20% improved. The vaginal exposure rate was 16% and no patient required reoperation for recurrent prolapse.[15]

In 2009, Natale and colleagues reported the results of an RCT studying Gynemesh PS and Pelvicol with two years of follow-up. They observed a 6.3% erosion rate in the Gynemesh PS patients, and four of the six of those patients underwent a concomitant hysterectomy. The cure rate for the Gynemesh PS cohort was 71.9%. Pre-operative pain was reported by 14 patients in the Gynemesh PS group and that dropped to 0 patients after surgery. Pre-operative dyspareunia was reported by 20 patients in the Gynemesh PS group, and that number dropped to 10 patients after surgery.[16]

Miller and colleagues, in 2011, reported the five-year results of 85 patients undergoing Gynemesh PS anterior and posterior repair with and without hysterectomy. The success rate in the treated compartment at five years was 77%, and the rate of mesh exposure was 19%. Before surgery, 21 patients reported unprovoked vaginal pain, 23 reported pain on examination, 15 had cystalgia, 24 had pain during Valsalva, and 46 had pain with prolonged standing. By five years, only one patient reported pain, which occurred on examination only. At five years, only one case of de novo dyspareunia was observed in those patients who were sexually active before surgery, while resolution of dyspareunia occurred in at least eight of twelve patients with pre-existing

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[12] Takeyama M, et al., Feasibility of the Tension-Free Vaginal Mesh Procedure Using Soft Polypropylene Mesh (Gyunemesh PS) in Japan. Int Urogynecol J 2007;18(Supp. 1):S25–S105 (Abs. 079).

[13] Al-Nazer MA, et al., Comparative Study Between Anterior Colporrhaphy Versus Vaginal Wall Repair with Mesh for Management of Anterior Vaginal Wall Prolapse. Int Urogynecol J 2007;18 (Suppl. 1):S25–S105 (Abs. 084).

[14] Caquant F, et al., Safety of Trans Vaginal Mesh procedure: Retrospective study of 684 patients. J Obstet Gynaecol Res 2008 Aug;34(4):449–56.

[15] Letouzey V, et al., Long-Term Results after Trans-Vaginal Cystocele Repair Using a Tension-Free Polypropylene Mesh. J Minimally Invasive Gynecol 2008;15:S1–S159 (Abs. 102).

[16] Natale F, et al., A prospective, randomized, controlled study comparing Gynemesh®, a synthetic mesh, and Pelvicol®, a biologic graft, in the surgical treatment of recurrent cystocele. Int Urogynecol J 2009;20:75–81.

dyspareunia. The authors concluded that the TVM procedure remains stable over time when measuring both quality of life and vaginal prolapse symptom scores.[17] Young-Suk Lee and colleagues in 2010 reported on their study of the treatment of 49 women undergoing transvaginal repair of pelvic organ prolapse with Gynemesh PS. They noted a 71.4% cure rate and an improvement rate of 18.4%. They observed only one vaginal erosion at the 12-month follow-up, which was asymptomatic. The authors concluded that "[t]rans-vaginal repair of an anterior vaginal wall prolapse with the monofilament polypropylene mesh Gynemesh™ PS is an effective and safe procedure."[18] Cuevas et al. reported in 2011 on a study involving the use of Gynemesh PS to create a Prolift-like device for treatment of severe pelvic organ prolapse. They observed a low recurrence rate, low rates of intraoperative and perioperative complications, and a low rate of mesh erosion. The study population was 100% satisfied with surgery, and 89.5% found the surgery improved their quality of life.[19]

Farthmann and colleagues studied 200 patients receiving either non-absorbable polypropylene mesh or a partially absorbable polypropylene mesh for cystocele treatment over three years. Consideration of mesh weight and foreign material were correlated with 200 patients randomized to conventional or a partially absorbable mesh. Management of mesh exposure, satisfaction with surgery, and postoperative pain were evaluated. Rate of mesh exposure was smaller in the partially absorbable mesh at 3.4% vs 7.5% at 36 months, but the authors found the rate of exposure to be low in both groups. Of the 200 patients, 27 patients had exposure of mesh, with 11 requiring surgical intervention. The rate of recurrent vaginal prolapse was higher in the partially absorbed mesh group. The mesh weight in the nonabsorbable group was 29 g/m^2 with porosity >75 µm. Interestingly, exposure rates varied from 0 to 20.4% between hospital groups, indicating that surgical technique is an important outcome-determining factor. Statistically significant risk factors for exposure uncovered were concomitant hysterectomy, smoking, cesarean section, and a longer incision. The authors concluded that use of synthetic mesh was a safe technique for treatment of pelvic prolapse. Patient satisfaction rates did not vary between the two groups.[20]

Samour and colleagues, in 2014, described the safety and efficacy of using Gynemesh PS for cystocele repair using a minimally invasive technique of transvaginal corkscrew application through the obturator foramen. 152 patients who underwent repair for cystocele grade 2 or greater using Gynemesh PS were followed for up to 36 months with a variable degree of dyspareunia observed in the first 3 months and marked improvement and even disappearance of pain for 90% of patients by the end of 6 months. 3% had persistent dyspareunia by the

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[17] Miller D, et al., Prospective Clinical Assessment of the Transvaginal Mesh Technique for Treatment of Pelvic Organ Prolapse—5 Year Results. Female Pelvic Med & Reconstr Surg 2011 May/Jun;17(3):139–43.

[18] Lee YS, et al., Efficacy and Safety of "Tension-Free" Placement of Gynemesh PS for the Treatment of Anterior Vaginal Wall Prolapse. INJ 2010;14:34–42.

[19] Cuevas R, et al., Prolift Like (PL) Surgery: A Management Option for Severe Pelvic Organ Prolapse (POP) in a Public Hospital in a Developing Country. Int Urogynecol J 2011;22 (Suppl. 2):S197–S1766 (Abs. 1108).

[20] Farthmann J, et al., Lower exposure rates of partially absorbable mesh compared to nonabsorbable mesh for cystocele treatment: 3-year follow-up of a prospective randomized trial. Int Urogynecol J 2013;24:749–58.

conclusion of the study. The rate of mesh exposure was 3.3%, reportedly due to the avoidance of excising vaginal epithelium and full-thickness dissection with lack of tension on the mesh. The authors concluded that transobturator placement of Gynemesh PS can be considered a minimally invasive and promising method for correction of cystocele and stress incontinence based on low rate of complications, high rate of success, and low incidence of recurrence.[21]

Dr. Marcus Carey and colleagues, in 2009, reported the results of a randomized controlled trial comparing anterior and posterior vaginal repair with Gynemesh PS augmentation or traditional anterior and posterior colporrhaphy. The success rate in the mesh group at one year post-op was 81%, but only 65% in the traditional anterior and colporrhaphy group. Patients had a high level of satisfaction with the surgery and both groups showed improvements in symptoms and quality-of-life data. New-onset dyspareunia was reported in 16% of sexually active women in the mesh group versus 15% in the non-mesh group.[22]

In 2006, Boulanger and colleagues published the results of a study in which they placed five different meshes—Vicryl, Vypro, Prolene, Prolene Soft, and Mersilene in the peritoneum of pigs to study the tissue integration and tolerance of the meshes. The authors found that the absorbable prostheses made of Vicryl and the non-absorbable prostheses made of polypropylene (i.e., Prolene and Prolene Soft) induced the least severe inflammatory reactions and produced the best tissue integration. They concluded that Type I Amid monofilament material, such as polypropylene, seemed to be the best integrated and tolerated.[23] Memon developed a biomechanical test to evaluate mesh-reinforced repair as compared to suture-reinforced repair in an animal model. The conclusion of the study was that Gynemesh PS was the least likely synthetic material to fail after repeated cycles of stressing, and was superior to xenograft-reinforced repair and to suture-only repair.[24] In an animal study published in 2007, Bhende and colleagues studied Prolene Soft and other synthetic meshes, as well as naturally derived meshes, to observe the extent to which the meshes served "as a nidus for microbial attachment and growth, thus exacerbating surgical site infection." They found that "[t]he synthetic meshes did not potentiate infection . . . whereas the naturally-derived meshes did."[25]

A 2013 study looked at how pelvic organ prolapse affects sexual function and found that the use of mesh in anterior compartment repair was not associated with a worsening in sexual function or an increase in de novo dyspareunia when compared to traditional anterior colporrhaphy.[26] Lowman and colleagues have reported that pelvic organ prolapse repair appears

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[21] Samour H, et al., Minimally invasive cystocele repair technique using a polypropylene mesh introduced with the transobturator route. Arch Gynecol Obstet 2015 Jan;291(1):79–84.
[22] Carey M, et al., Vaginal repair with mesh versus colporrhaphy for prolapse: a randomised controlled trial. Br J Obstet Gynecol 2009 Sep;116(10):1380–1386.
[23] Boulanger L, et al., Tissue integration and tolerance to meshes used in gynecologic surgery: An experimental study. Eur J Obstet & Gynecol and Reprod Biol 2006;125:103–08.
[24] Memon HU, et al., Comparison of graft-reinforced repairs and suture repair using a novel biomechanical test
[25] Bhende S, et al., Infection Potentiation Study of Synthetic and Naturally Derived Surgical Mesh in Mice. Surg Infections 2007;8(3):405–14.
[26] Dietz V and Maher C, Pelvic organ prolapse and sexual function. Int Urogynecol J 2013;24:1853–1857.

to have a high rate of associated dyspareunia regardless of whether the surgery is performed transvaginally or transabdominally.[27]

Ongoing technological advances of synthetic meshes using polypropylene have been a moving target, with development of lighter and less stiff materials over the last 10 years. At the time of introduction of Gynemesh PS in the early 2000s, the material was considered the least stiff and most porous mesh to receive FDA clearance and introduction into the surgical market. The stiffness, weight, and porosity of Gynemesh PS has subsequently moved to the middle of the spectrum of synthetic mesh products as recent science has favored the least stiff, lightest weight, and most porous material possible. Nonetheless, Prolene Soft mesh is still a lightweight, large-pore mesh. There is a point of diminishing returns, as some of the lightest weight meshes have the most deformation and can fail in the physiologic environment of the vagina. Complications that are described are more related to surgical technique and patient selection than the individual mesh product used. The avoidance of large and "T" incisions, concomitant hysterectomy, tobacco use, obesity, exposure to radiation therapy for pelvic cancer, chronic use of steroids, and advanced age all play a significant role in the incidence of vaginal mesh exposure. Injury to either bladder intestine or rectum is a direct result of surgical misadventure. Patients with symptomatic and increasing vaginal prolapse who have failed previous native suture plication often require augmented repairs with xenograft or synthetic materials.

I have personally performed over 1,000 procedures involving implantation of Prolene polypropylene mesh for treatment of stress urinary incontinence or pelvic organ prolapse, and have found the Prolene polypropylene products to be safe and efficacious when following the appropriate patient selection and the technique described by the product instructions for use and sound medical judgment and surgical technique and concepts. I have lectured and proctored physicians on the safe use of Prolene polypropylene devices for pelvic floor surgery since the early to mid 1990's. The devices were the highest quality for the day and advanced appropriately over time. They were straightforward, and the polypropylene mesh was stable over time and used for hernias over 60 years, I have patients implanted over 20 years ago and see no long-term complication trends. Since the television advertisements claiming pelvic mesh is a dangerous product, I have received hundreds of phone calls from anxious patients with fears of product recalls and future complications. The overwhelming majority of those anxious patients have excellent outcomes and no adverse symptoms. The effect on current patients is to create fear that a synthetic sling will cause future problems and many choose not to proceed to treatment. There is a 30% reduction in the number of patients undergoing stress incontinence and pelvic reconstructive surgery.[28] As set forth above, the efficacy and safety of the Ethicon's Prolene Soft mesh is well-reported. It was incorporated into Ethicon's Prolift device, which was the most studied mesh kit for pelvic organ prolapse treatment, and again, the studies showed high

[27] Lowman JK, et al., Does the Prolift system cause dyspareunia? Am J Obstet Gynecol 2008;199:707.e1–707.e6.

[28] Perkins CE, Warrior K, Eilber KS, et al. The Role of Mid-urethral Slings in 2014: Analysis of the Impact of Litigation on Practice. Curr Bladder Dysfunct Rep (2015) 10:39-45. DOI 10.1007/s11884-014-0278-z; Koo K, Gormley EA, Abstract MP81-05: Transvaginal Mesh in the Media Following the 2011 FDA Update.

success rates with minimal complications.[29] The peer-reviewed, published clinical data shows that procedures involving Prolene Soft mesh can be performed safely and effectively. The studies show that most patients do not experience dyspareunia or pelvic pain after undergoing transvaginal mesh repair for pelvic organ prolapse and this was my experience.

Additionally, the professional organizations AUGS and SUFU—non-profit organizations representing over 2,000 practicing physicians, nurse practitioners, physical therapists, nurses, health care professionals and researchers dedicated to treating female pelvic floor disorders—have made the following statements regarding the safe use of polypropylene and the benefits of providing surgeons with options for treating pelvic floor disorders:

Polypropylene material is safe and effective as a surgical implant. Polypropylene has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades, in millions of patients in the US and the world (personal communication with manufacturers of polypropylene suture and mesh). As an isolated thread, polypropylene is a widely used and durable suture material employed in a broad range of sizes and applications. As a knitted material, polypropylene mesh is the consensus graft material for augmenting hernia repairs in a number of areas in the human body and has significantly and favorably impacted the field of hernia surgery. As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years.[30]

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The American Urogynecologic Society strongly opposes any restrictions by state or local medical organizations, healthcare systems, or insurance companies which

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[29] Halaska M, et al., A multicenter, randomized, prospective, controlled study comparing sacrospinous fixation and transvaginal mesh in the treatment of posthysterectomy vaginal vault prolapse. Am J Obstet Gynecol 2012;207:301.e1–7; da Silveira S, et al., Multicenter, randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse surgical treatment. Int Urogynecol J 2015 Mar;26(3):335–342; Svabik K, et al., Comparison of vaginal mesh repair with sacrospinous vaginal colpopexy in the management of vaginal vault prolapse after hysterectomy in patients with levator ani avulsion: a randomized controlled trial. Ultrasound Obstet Gynecol 2014 Apr;43(4):365–371; de Landsheere L, et al., Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up. Am J Obstet Gynecol 2012 Jan;206(1):83.e1–7; Withagen MI, et al., Trocar-Guided Mesh Compared With Conventional Vaginal Repair in Recurrent Prolapse: A Randomized Controlled Trial. Obstet Gynecol 2011 Feb;117(2):242–250; Sokol AI, et al., One-year objective and functional outcomes of a randomized clinical trial of vaginal mesh for prolapse. Am J Obstet Gynecol 2012 Jan;86:e1–e9; Altman D, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011;364:1826–1836.

[30] AUGS-SUFU, Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 3, 2014).

ban currently available surgical options performed by qualified and credentialed surgeons on appropriately informed patients with pelvic floor disorders.[31]

I agree with these position statements.

The theory of mesh degradation is not substantiated in the literature or in my personal experience using polypropylene slings and mesh for incontinence treatment and pelvic reconstruction. Studies of explanted mesh are difficult to interpret, as there is damage to the material during explantation, treatment with chemicals to remove the collagen and biologic matrix that has incorporated into the mesh, and preparation onto slides for microscopic examination. There is no literature to support clinically significant mesh degradation in humans. Polypropylene suture and mesh has been utilized for over sixty years from vascular, cardiovascular, Gynecology and general surgery with no connection to breakdown or cancer association in humans.

Nor have I seen a problem with Prolene Soft or any other Prolene mesh roping or curling, unless it is placed improperly by over-tensioning. Nor have I observed particle loss from mechanically manipulation of the mesh in my practice. Furthermore, the mesh does not shrink, its the scar tissue that forms after any pelvic surgery that contracts, and tissue incorporating into implanted mesh is no exception, but the mesh itself does not contract. Prolene is inert.

Some plaintiffs' experts' have said that placement of transvaginal mesh is dangerous and violates one of the most basic tenets of surgical teachings in that it involves placing a permanent implant into a human through a contaminated surgical field. If that theory was correct, the majority of patients receiving transvaginal mesh would have infections. However, vaginal infections following implantation of transvaginal mesh are very rare. For that matter, all vaginal surgery would have this issue especially human issue like fascia used in autologous slings would all be massively infected and they are not. The pore sizeallows the body's own mechanisms to clean and heal through the graft and is the advantage over the avascular autologous implants. In my experience in 1000's of graft placements the infection rate is lower than vaginal cuff infection from a hysterectomy.

There are also claims that Prolene Soft mesh is cytotoxic and causes an excessive inflammatory response. This is not supported in the literature, and I have not seen it in my practice.

Plaintiffs' experts claim that mesh made of Prolene polypropylene is carcinogenic, but there is no reliable scientific evidence to support the theory or claim that polypropylene can cause cancer or sarcoma. In the more than 1,000 cases in which I have implanted one of the Ethicon as well as other companies Prolene polypropylene products, I have not seen a single case of cancer attributable to the mesh or suture. The literature also refutes plaintiffs' experts' suggestion or claim.[32] .)

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[31] AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders (2013).

[32] King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; Moalli P, et al., Polypropylene mesh: evidence

V. Prolene Soft Mesh's Instructions for Use and Other Educational Materials

a. Ethicon's Instructions for Use

The instructions for use (IFU) accompanying the Prolene Soft mesh note that the mesh "may be used for the repair of hernia or other fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result." It is not specifically indicated for pelvic floor repairs, but is generally indicated for, among other things, repair of fascial defects. It warns that use of the mesh in contaminated wounds may result in a subsequent infection requiring removal of the mesh. It also notes that the potential adverse reactions associated with the mesh "are those typically associated with surgically implantable materials, including infection potentiation, inflammation, adhesion formation, fistula formation, and extrusion." It also provides instructions for the placement of nonabsorbable sutures at a certain distance apart from one another and away from the edge of the mesh when suturing the mesh to tissue. These instructions for use and the warnings contained therein are adequate and allow for the safe use of the device. The instructions are such that a trained and experienced physician could implant the mesh safely and effectively. The IFU is not intended to teach surgical technique, which is assumed to have been in the skill set of the surgeon. Every surgeon should be aware of the intraoperative and post-operative risks inherent in the use of surgical mesh. A surgeon need not be taught the entire practice of medicine in an IFU. The totality of surgical risks is not included in the IFU for surgeons. Surgeons have training from numerous sources—medical school, residency, maybe fellowships, colleagues' experiences, their own experience, literature, etc. The IFU is used by the surgeon to become familiar with the specific device, the handling, placement and deployment in the manner that maximizes safety and efficacy. The IFU is never assumed to be a completely comprehensive list of all the possible adverse complications that are low prevalence. The IFU is intended to guide the surgeon to perform the procedure as the device was designed. In my opinion, the IFU for Prolene Soft, like that for Gynemesh PS which is specifically indicated for pelvic floor repair, is adequate to inform and warn a pelvic surgeon of risks with the device.

Mesh exposure and erosion or extrusion are the only unique risks to mesh surgeries, and are essentially wound complications. However, permanent sutures (Gortex, ethibond, prolene, etc.) also can be exposed, erode or spit (extrude) as well and are common occurrences in prolapse surgery. Wound complications can also occur with other surgeries. Mesh exposure can be caused by poor quality tissue due to atrophic vaginitis, poor blood supply, history of pelvic radiation therapy, too superficial dissection prior to placement of slings mesh or sutures, hematomas, tobacco usage, and early sexual activity.

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for lack of carcinogenicity. Int Urogynecol J 2014, DOI 10.1007/s00192-014-2343-8; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453; Brian J. Linder ,et al Mayo Clinic, Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence, Int Urogynecol J, Feb 10, 2016.

Plaintiffs' experts may claim that pain, dyspareunia, voiding dysfunction, and the need for cystoscopy during cystocele repair should have been warned about in the IFU. I disagree. Pelvic floor surgeons know that pain and dyspareunia may occur with any pelvic floor surgery, and that voiding dysfunction and bladder injury may occur with cystocele repair. Surgeons need not be specifically warned in an IFU of these fundamental surgical risks. Published data supports the fact that dyspareunia rates following pelvic floor surgery with Prolene Soft mesh are low.[33]

VI. The Design of Prolene Soft Mesh

a. The Usefulness, Desirability, and Safety of the Prolene Soft Mesh

Prolene Soft mesh is very useful to surgeons because it is a lightweight, large-pore, knitted, monofilament Prolene polypropylene mesh that is well-tolerated by the body and adds needed reinforcement to native tissue for repair of fascial defects. The large pore-size of the mesh allows for tissue incorporation and the passage of macrophages and leukocytes to help clear any bacteria that could lead to an infection. The mesh can be cut to any shape and can be trimmed to fit individual patient anatomy. Unlike allograft or xenograft material, synthetic mesh like Prolene Soft is readily available, is not met with cultural or religious objections, and presents no risk of disease transmission by viruses, prions, and bacteria.

The polypropylene monofilament used to knit the mesh has been safely used in surgery as suture throughout the body for over 50 years, and has been shown to be stable and does not degrade in the body over time. The mesh is also useful because it comes with instructions for use, a tracking lot number for safety and batch analysis, as well as MDR reporting and FDA analyses. The mesh is not met with cultural or religious objections like allografts or xenografts, and is extremely effective and durable, with very low recurrence rates. As discussed in the studies above, there is an extensive body of literature supporting the safety of the mesh and the efficacy of treating pelvic organ prolapse with the mesh.

It is comforting as a surgeon to be using a product that is known to have the largest amount of peer-reviewed data from multiple institutions substantiating a safe, reliable, reproducible technique and material. Prolene has been around for 50 years, been safely used in various applications, and the body's reaction to the material is known.

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[33] Fatton B, et al., Transvaginal repair of genital prolapse: preliminary results of a new tension-free vaginal mesh (Prolift™ technique)—a case series multicentric study. Int Urogynecol J 2007;18:743–752 (noting that among the 30 patients known to be sexually active, 76.6% had resumed sexual intercourse at three months follow-up, while only three patients complained of dyspareunia); Paplomata E, et al., Genital Floor Repair Using Polypropylene Meshes: a Comparative Study. 2007 (Abs. 482) (noting that only two patients of 56 that underwent prolapse repair with Gynemesh or Prolift developed dyspareunia during 21-month follow-up); Jacquetin B, et al., Total transvaginal mesh (TVM) technique for treatment of pelvic organ prolapse: a 5-year prospective follow-up study. Int Urogynecol J 2013 Oct;24(10):1679–1686.

Complications are usually surgery-related and not mesh-specific. Extensive exposures are uncommon and manageable, occurring in a small minority of cases. The cause can be poor tissue integrity caused by estrogen deficiency, delayed wound healing due to diabetes, steroid usage, hematoma formation, or placing the sling too superficially. Treatment includes application of topical estrogen cream, re-closure of the mucosal edges, and limited mesh excision if necessary. The excision can be performed in an office setting under local anesthesia or under light sedation in an OR. Dyspareunia is rare following implantation of the mesh and in my hands can be treated in the office with less than 1% with some persistent pain. Most sexual dysfunction occurring after pelvic organ prolapse surgery is connected to concomitant hysterectomy and/or oophorectomy with lack of Estrogen replacement. Graft-related complications can occur with any material used for augmentation, whether it is synthetic or biologic graft material or synthetic suture material.

All surgical procedures have inherent risks. All pelvic surgeries have similar risks, and the introduction of the Prolene PS mesh has served to decrease complications when compared to previous techniques. Because native repairs do not involve a kit product, complications are not reportable to the MAUDE database. Scientific research has provided improved materials and applications to both improve efficacy and decrease complications. Synthetic mesh that is microporous or too macroporous has proven to be either less safe or less efficacious. If the mesh is too lightweight or too large pore, there is inadequate support.

All pelvic surgery has similar and inherent risks. Pelvic floor surgeons should be and are aware of the potential complications involved with any surgical treatment of pelvic organ prolapse based on a combination of their medical school education, their residencies, fellowships, their experience, their continuing education, and their review of the surgical mesh's IFU if a surgical mesh is used. Risks such as infection, scarring, inflammation, bladder damage, bowel damage, ureter damage, nerve damage, injury to vessels, wound complications (such as wound dehiscence, herniation, hematoma, seroma, pelvic abscess, exposure, and erosion), pain, pelvic pain, groin pain, dyspareunia, fistula, anesthetic risks, bowel or bladder dysfunction, failure of the operation, bleeding, death, pulmonary embolism, myocardial infarction, pneumonia, deep vein thrombosis, and need for reoperation are basic elemental surgical risks of any pelvic floor surgery involving mesh. Surgeons understand that these complications can happen, and they also understand that the symptoms can range in terms of severity and duration.

Surgeons are expected to understand the anatomy in which they are operating, and should identify and dissect in safe planes, avoiding inadvertent damage to the organs and vessels contained within the pelvis. The education and training of the pelvic surgeon should be adequate to know the possibility of complications and their avoidance, risks of recurrence and reoperation. Indeed, the development of biologic and synthetic materials was motivated by the high failure rate of pelvic reconstruction due to the weakness of the patients' connective tissue leading to the condition requiring repair. There is an extensive body of medical knowledge in the medical literature discussing the possibility of complications with the use of meshes. Surgeons' prior experience with mesh informs their understanding of potential complications with pelvic floor surgeries, including those involved with mesh devices. While mesh exposure is unique to mesh devices, it is obvious, and it is general knowledge within female urology and urogynecology.

The potential injury to vessels and organs caused by trocars is well-known to surgeons, and potential mesh exposure and foreign body reactions are common knowledge.

Furthermore, the FDA issued a Public Health Notification in 2008 regarding the use of synthetic mesh for treatment of prolapse and incontinence. It alerted healthcare practitioners to "complications associated with transvaginal placement of surgical mesh to treat Pelvic Organ Prolapse (POP) and Stress Urinary Incontinence (SUI)." It noted that the major complications were rare, but could have serious consequences, and that the "most frequent complications included erosion through the vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence." It also noted that there were "reports of bowel, bladder, and blood vessel perforation during insertion," and that "in some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia." This Public Health Notification was yet another source of knowledge for surgeons regarding potential complications associated with synthetic mesh and midurethral slings, complementing the TVT and TVT-O's IFU, Ethicon's professional education seminars, and the surgeons' training, education, and experience.

Based upon the analysis above, and on my education, my training, my experience using these products and alternative incontinence treatments, and my reading of the literature referenced above, I believe that Ethicon's Prolene Soft / PS mesh is not defective, but is reasonably safe for its intended use and has a positive benefit-to-risk profile. In my opinion, the benefits of the Prolene Soft mesh far outweigh the risks of using the product. At the time the products were launched, I do not believe they could have been made safer for their intended use. The products were state of the art at the time they were launched, and remain so today.